Industrial College of the Armed Forces
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Biotechnology

Abstract

The United States is the world leader in the biotechnology industry in all aspects and biotechnology is quickly becoming a major industrial player in the U.S. and globally. The biotech arena touches multiple facets of a number of industries: medicine, agriculture, aquaculture, forestry, defense and others. Biotechnology is still an immature industry that has yet to reach its potential, but will likely have an impact on almost every aspect of the U.S. economy and our way of life in the future. With the mapping of the human genome, medical discoveries occur daily – pure science, new medicines, and genetically enhanced products designed to save lives. Biotech agriculture is a possible solution in the face of increasing global population to food shortages that will not be met by the "Green Revolution" of the past century. Biotechnology holds promise for a cleaner environment through genetically engineered plants and targeted bioremediation. Biotechnology is greatly affected by government investment in basic science, regulation, and product approval processes – which drives a unique business model. While the U.S. is the world leader, international competitors are gaining ground. Biomedical technologies have the potential to relieve human suffering and solve a range of societal problems. However, some of these technologies are controversial, such as stem cell research and cloning) and raise ethical, moral and social issues. Potential dual use of biotechnology complicates the effort to craft effective non-proliferation policies and mitigate bio-weapons threats. Biotechnology has the potential to revolutionize all aspects of our daily of life over the next two decades, in much the same way information technology did during the previous two decades.

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"The biotechnology industry finds itself on the front lines of some of the greatest challenges of our time." President George W. Bush, 23 June 2003

INTRODUCTION

Biotechnology is quickly becoming a major industrial player not only in the United States, but globally. The biotech arena touches multiple facets of a number of industries: medicine, agriculture, aquaculture, forestry, defense, and others. Why study biotechnology? The White House designated biotechnology a "National Critical Technology" because of its significant impact on U.S. national security. No other single industry today has the same potential to impact our lives on a similar scale. With the mapping of the human genome, medical discoveries occur daily – pure science, new medicines, and genetically enhanced products designed to save lives. Biotech agriculture is a possible solution in the face of increasing global population to food shortages that will not be met by the "Green Revolution" of the past century. Biotechnology holds promise for a cleaner environment through genetically engineered plants and targeted bioremediation. The United States is the world leader in the biotechnology industry in all aspects – the number of companies, size of research base, number of products and patents, and level of revenue. In the course of our study of this industry, we discovered several common themes that have a significant impact on the U.S. biotech industry:

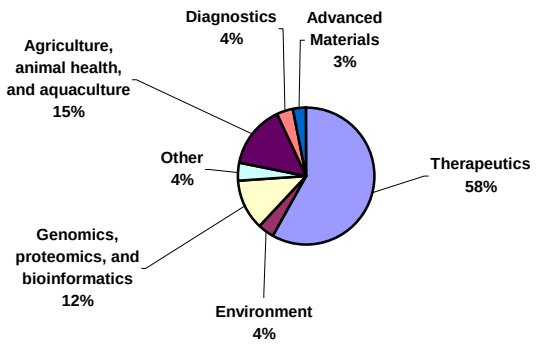
- Biotechnology is still an immature industry that has yet to reach its potential, but will likely have an impact on almost every aspect of the U.S. economy and our way of life in the future
- Biotechnology is greatly affected by government investment in basic science, regulation, and product approval processes – which drives an unique business model
- The U.S. is the world leader, but international competitors are making significant investments to become global players
- Potential dual use of biotechnology complicates the effort to craft effective non-proliferation policies and mitigate bio-weapons threats
- U.S. future lead in biotechnology is threatened by a potential shortage of U.S. scientists and engineers, an increasing global demand for scientists, fewer U.S. college graduates in math and science, and tighter U.S. visa restrictions on foreign students and scientists

This paper will provide a broad assessment of the nature and overall strength of the U.S. biotechnology industry, the impact of government policies and regulation, and recommendations for future U.S. policy. The paper will address the definition and current state of the industry, the industrial application of biotechnology in medicine, agriculture, environment, and bio-defense, the global biotech industry and the future of the biotech sector.

INDUSTRY DEFINED

There is no single, easy definition of "bio-technology". Rather, it is more an "umbrella term that covers various techniques for using the properties of living things to make products or provide services."[i] The U.S. Department of Commerce defines biotechnology as "...a diverse collection of technologies that manipulate cellular, sub cellular, or molecular components in living things to make products, discover new knowledge about the molecular and genetic basis of life, or modify plants, animals, and microorganisms to carry desired traits..." [ii]

Figure 1: 2002 Distribution of biotech companies by sector



The biotechnology industry is complex. The industry crosses many disciplines and thus it is difficult to obtain definitive data to compare in most common databases. The U.S. uses the "North American Industrial Classification System (NAICS)" to identify specific products but does not provide distinct codes for biotechnology-derived products. For example, the US does not differentiate between genetically engineered agriculture and "natural" agriculture therefore the data are combined into one category. Additionally, the biotech industry is "science heavy", that is, across the various disciplines the one constant is the absolute reliance on scientific research and innovation.

The biotech industry consists of a number of related but distinct application areas including pharmaceuticals and vaccines, medical diagnostics, agriculture and foods, animal health, environmental management, industrial applications, and forensic testing. Figure 1 shows the relative use of biotech in sector areas for 2002.

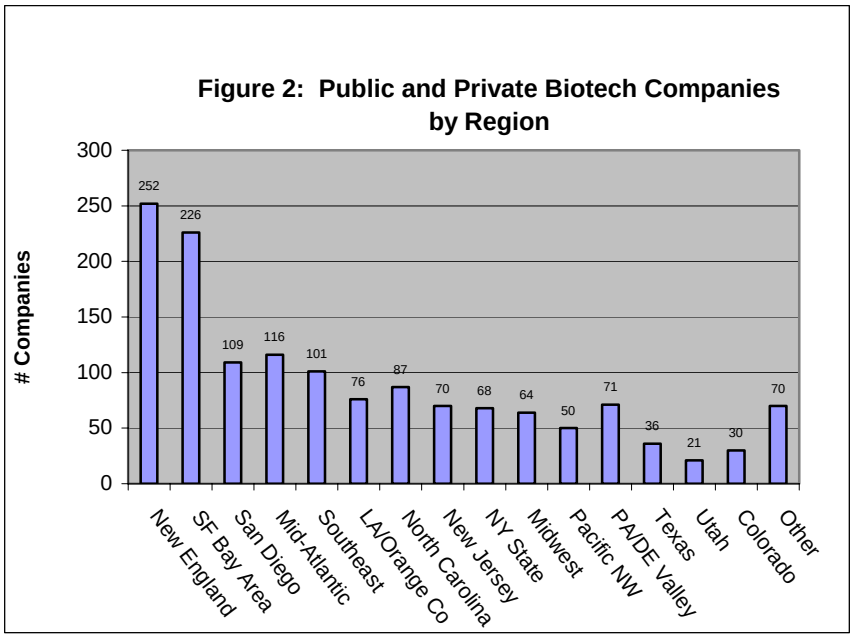
CURRENT STATE OF THE INDUSTRY

Industry Overview - Biotech firms range from "small, dedicated biotech companies that are R&D-intensive and operate primarily on venture capital, grants, initial public offerings (IPOs) and collaborative agreements, to large, diversified companies that have greater in-house resources and well-established production and distribution systems."[iii] The majority of firms are clustered within 12 states primarily due to the synergy afforded from the collocation of industry and academic institutions. California boasts the largest contingent of biotech companies, with nearly 450 firms. This is more than double the number of runner-up Massachusetts (figure 2).[iv]

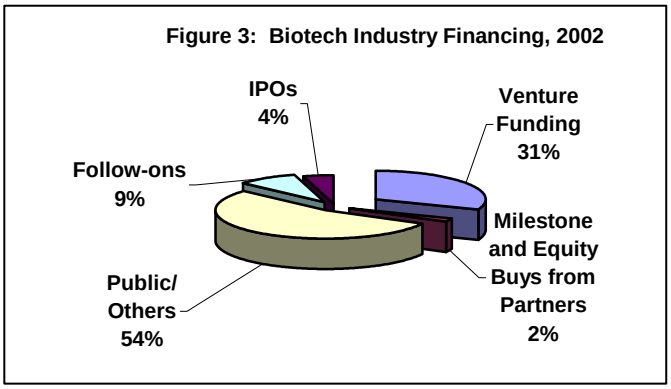
Globally, nations approach the biotechnology market within two distinct strategies. Some nations have a strong focus on basic scientific research to discover new applications and develop new processes that can then be applied across the various sectors of the industry, while other nations focus more on the exploitation of existing technologies to

discover new product lines. The United States falls into the former camp, with a strong commitment to research and development, which has led to some of the most important scientific achievements of the 20th century, such as the mapping of the human genome.

Financial Status - The stock market decline in 2000-2001 and subsequent U.S. recession hit the biotech industry hard in terms of available investment capital and overall market capitalization.[v] In spite of these setbacks, the biotech industry continues to show strong growth in revenues, sales, and job creation and is displacing all other market sectors, including software development, as the top priority for investors.[vi] This recovery is due in large part to continued heavy investment by the U.S. Government in basic biotech R&D through the recession period, as well as the successful commercialization of more biotech products than ever before. At the same time, scientists are experiencing a rapid acceleration of product development as they exploit the power of information technology on a broadened life science knowledge base[3].



Financing - Biotech, more than any other U.S. industry, requires large up front capital investments in R&D to bring new products to the market. R&D costs comprise half of the annual revenue in traditional biotech firms.[vii] Biotech companies rely on a variety of means to finance these large up front capital requirements including government financing, venture funding, private funding and Initial Public Offers (IPOs) (Figure 3). For example, the National Institute of Health (NIH) is the largest federal R&D sponsor, and while the biotech industry conducts some basic research, "it relies on NIH and its grantees to conduct the majority of research". [viii] Increasingly, state and local governments are using a combination of grants and tax relief to lure biotech jobs into their areas and to form research "clusters" between industry and academic institutions. Biotech claimed the top spot for venture capital in 2003, overtaking software development, attracting $4.89B, or 27% of all venture capital.[ix] At the same time, this venture financing also shifted towards later stage development, probably as a result of the cautious nature of venture financiers in the wake of the stock bubble burst of 2000/2001.[x] Private financing plays an important part, especially for



smaller firms, and enables firms to pursue products or methods that the government would not support through grants due to ethical or political considerations (e.g. stem cell research). Finally, biotech firms used Initial Public Offerings in great numbers to generate capital prior to the stock market collapse in 2000. The problem for investors is the long lead times necessary to develop a successful product, which may take up to 15 years to get to market. Even so, the Standard & Poor's (S&P) Biotech Index has posted an average annual gain of 19.8% for a five-year period ending October 24, 2003.[xi]

INDUSTRIAL APPLICATIONS:

Medical - The human health sector represents over 70% of the biotech industry. Biotech drugs and medical procedures promise blockbuster results by improving diagnostic practices and extending human life spans. As of October 2003, the Federal Drug and Administration (FDA) has approved more than 155 biotech drugs and vaccines, while yet another 370 are still in various stages of clinical testing.

As a percentage of revenues, research and development in biotech is higher than other industry sectors. In 2002, biotech R&D spending was $12.5 billion--an increase of $2.3 billion over the previous two years. A survey by the Department of Commerce indicated "...biotechnology-related activities accounted for 26% of capital investments and 40% of R&D expenditures, but only 15% of annual net sales and 14% of operating income in 2001." As more products reach the market, the large gap between R&D and revenues will decrease.[xii]

Although the time to develop and get a drug through the FDA varies, the average time for a biotech drug is 10 to 15 years. The average cost to get a drug through the entire process is $880 million. This cost includes the drug discovery process, the clinical process, and the drug failures along the way to develop the final drug. Drug development failures, i.e. the number of products that do not make it through all stages of the testing and approval process, represent approximately 75% of the overall cost.[xiii] The purpose and goal of the FDA approval process is to ensure both the health and safety of the recipients and the overall efficacy of the new drug in the treatment of a specific illness. This 10-15 year testing and approval process involves three phases. In the first phase, the drug is administered to a small healthy population to ensure the drug is safe. In Phase II, the drug is given to patients who actually are suffering from the target illness or condition, thus determining if the drug is effective (efficacy). In Phase III, a larger population of patients is tested and monitored for safety and efficacy. The FDA estimates that for every 20 drugs that enter clinical testing, only 13 drugs make it through Phase I. Of those, only nine drugs will make it through Phase II and on average, only one or two of those make it through Phase III. Therefore, only 5% to 10% of the initial drugs entering clinical testing make it through the entire process. [xiv] Even more striking, only a small percentage of those approved actually become profitable in the commercial market. Even so, pharmaceuticals ranked first in profits in 1999, since many of those that do succeed end up as blockbuster products with large profit margins.[xv]

Most biotech companies have no experience in manufacturing their final product. Producing a drug in the lab is much different from manufacturing the product in commercial cost-effective quantities. Consequently, most biotech firms rely on third-party companies or collaborate with large pharmaceutical companies to manufacture and market their products.

In order to be forward thinking, biotech companies should plan the manufacturing strategy while products are proceeding through clinical trials. Since a patent may have already been initiated in early clinical testing, companies must ensure their product is ready for immediate production once clinical testing is complete. By doing so, the product will not be delayed in production once the FDA approves their drug. This strategy has significant risk, since a company is dependent on the successfully performance of the drug in clinical trials and subsequent wide acceptance of the product by consumers. Companies must take maximum advantage of their patent protection and must have a manufacturing plan ready in order to maximize potential profits once FDA approval is received.[xvi]

Government plays a significant oversight role in the medical biotech industry. The drug approval process through FDA and the patent protection laws are the primary means of regulating the industry. In addition, the government provides special funding and incentives for non-marketable drugs such as vaccines. The government must continue to invest and provide resources and incentives for military specific drugs, like vaccines. If not, vaccines or other drugs directed at smaller populations will never be developed.

Many small companies are merging with larger biotech firms or large pharmaceuticals in order to ensure they have appropriate working capital. By using this strategy, biotech companies can ensure products are in different phases of development and in production to generate revenues. Companies that are successful in marketing profitable drugs can be more self-sustaining for their continued research and discovery of future drugs.[xvii]

Current trends in the biotech industry indicate large pharmaceutical companies and even other biotech firms looking to buy/license products/technologies from small R&D biotechs once a product shows market potential. By doing so, companies can minimize the risks and focus on the final development, manufacturing, and marketing.

Medical biotech companies have a legitimate case for the high prices of their drugs and technologies due to the length of time and large capital investment often required to bring a product to market. However, there is public sensitivity to high priced medical products that biotech companies must consider in their pricing strategies. Again, a balance must be achieved so that the industry is rewarded for innovation, while at the same time; the overall health of the U.S. is continually improved by allowing maximum access to biotech drugs.[xviii]

Agriculture - The United States is by far the world's leader in this industry. Ninety-nine percent of the world's plantings of genetically modified (GM) food and feed crops are restricted to just four countries: the United States, Canada, Argentina, and Brazil, with China rapidly joining the fray.[xix] Six multinational companies dominate the market: Astra-Zeneca, Aventis, Dow, Dupont, Monsanto, and Novartis.[xx] The U.K. biotechnology sector

boasts 400 biotech firms, employing 25,000 people. The U.K. has the largest biotechnology sector in Europe and is second only to the US worldwide.[xxi]

The bio-agriculture industry currently has three major product lines. The first and arguably most important use of genetic modification in plant agriculture is herbicide tolerance,[xxii] which accounts for 77% of genetically engineered crops planted.[xxiii] This process genetically modifies the composition of plants to make them resistant to damage from the chemical herbicides used to kill weeds. Monsanto Company is the leading US company, producing almost all the new genes that are in commercially grown genetically engineered (GE) crops.[xxiv]

The second major product line is an insect resistance crop, which accounts for approximately 20% of GE crops. A plant is genetically modified to include a naturally occurring but lethal gene that kills insects when they attempt to eat the plant. This process reduces farmers' expenses for insecticides, helps keep the environment clean by reducing the use of pesticides, and increases crop yield.[xxv]

Genetically modified seed is the third product line. The US industry started selling GM seeds in 1996 and the acreage planted with GM seeds has increased 30 times since then. Globally, bio-agriculture accounts for a small share of all agricultural production - approximately three percent. However, in the four main crops (soybean, cotton, canola, and corn), the portion planted with GM seeds comprises 19 percent of the world's total acreage. The U.S. Department of Agriculture reports that US use of genetically modified seeds for corn, soybean, and cotton will be 32%, 74%, and 71% respectively of total US acreage by 2005.[xxvi] Notably, in 2001 US farmers saved $1.4 billion by using these four GE crops due to lower chemical and other input costs.[xxvii]

Public acceptance is a major hurdle for the bio-agriculture industry. In the US, many farmers are debating whether or not to grow genetically engineered crops for fear of consumer and market rejection of their products. The US is the world's leading agriculture exporter. However, if foreign markets, such as the EU, are closed to genetically engineered crops – then farmers will plant what they can sell, and it won't be genetically engineered. Along the same lines of concern comes the issue of labeling which is discussed later in the paper.

The U.S. government regulates the bio-agriculture industry through a triad of agencies: the USDA, FDA, and EPA. The majority of government regulations exist to ensure that genetically engineered crops are tested safely with no danger to the surrounding ecology as well as to ensure that crops grown for animal feed do not end up on your dinner table – which has happened in the past. The government agencies are working with the industry to ensure market safety while not hampering innovation and progress.

In addition, it is worth noting the future potential of biotech agriculture. In order to make the industry more profitable, the industry is examining ways to improve "output traits" or making the products more appealing. Imagine trying to get your three-year-old to eat his spinach if it tasted like ice cream! One of the recent discoveries is the genetic

enhancement of rice in order to add nutritional value by enabling the production of beta-carotene, the vitamin A-precursor, in the rice grain. Additionally, genetically enhanced food can be used as a medicinal delivery system. Adding healthy, nutritional or medicinal benefits to bio-agriculture may help enlarge the US market.

Environmental - Environmental biotechnologies can be defined as any use or manipulation of biological materials that reduces wastes and improves the quality of the environment.

Bioremediation is the use of bacteria to transform hazardous wastes into non-toxic or less toxic substances. It has proven successful in the remediation of polluted air, land and water. It covers a wide variety of applications, though most commonly it is divided between "in-situ" and ex-situ" techniques. There are approximately 400,000 hazardous waste sites in the U.S. [xxviii] Dealing with hazardous waste sites using conventional physio-chemical technologies is estimated to cost $1.7 trillion dollars in the United States alone. Additionally, the most common of these technologies either move the pollutants to another medium (ground to air), or concentrate and move it to another location (landfilling). The promise of bioremediation is that of significant cost reduction (by as much as an order of magnitude), less site disturbance, and transformation of many pollutants to harmless material.

The concept of bioremediation is not particularly new to the environmental remediation market, yet despite its enormous potential for cost savings, it has not captured as large a share of that market as one would expect or some scientists would hope. The commercialization of the process has not kept pace with the technological improvement. It is estimated to be approximately 2-10% of the market for remediation. Growth rates are estimated anywhere from 15-25% annually. A number of factors have limited greater growth and market share, including slow acceptance by regulators who are under pressure from the public to clean up sites quickly; slow public acceptance due to concerns regarding the introduction of genetically modified (GM) GM microbes; and lack of large scale demonstrated success as most bioremediation activities are still reported as "demonstration projects" and most of those are projects are at Federal government sites.

Environmental industrial applications have often been referred to as biotechnology's third wave (after pharmaceuticals, agriculture) with enormous as yet untapped potential. Bioproducts (goods manufactured wholly or in part from renewable biomass) range from paint and adhesives to detergents, inks, paper, absorbents and building materials. The 2002 Farm Security and Rural Investment Act includes provisions designed to stimulate the industry through requirements that federal agencies' procurement practices favor biobased products. Although implemented in December 2003, it will take a few more years for the full impact to be realized. The U.S. market for disinfectant and anti-microbial chemicals and the market for biofilms in paints and coating are both projected to reach $700m by 2005.[xxix] Additionally, bioenzymes and biocatalysts offer great potential because they operate at lower temperatures, produce less toxic waste, fewer byproducts and less emissions than conventional chemical processes. Bioenzymes are added to animal feed to increase digestibility and nutritional value, paper production as a substitute for

more toxic chlorine, mining to extract precious metals from ore (in lieu of cyanide), textiles, detergents, fuel production, and brewing. The U.S. market in 2000 was estimated to be about $515m growing at 4.1%. The current total global market is between $1.6-$2 billion.[xxx]

Environmental biotechnology will provide alternatives to industry as natural resources become increasingly scarce. The United States is uniquely positioned to harness this technology but the promise of environmental biotechnology extends beyond our own national security to global energy use, climate, and air, water and land quality.

The U.S. dependence on foreign energy sources shapes our national security strategy. Biomass fuels can provide a viable alternative and can be used to diversify our current fossil based energy dependence and reduce our vulnerability to disruptions of the energy supply. There are a multitude of different fuel types such as biodiesel (developed from soy or animal fat) and ethanol/methanol (developed mostly from corn). Technology has been developed to retrofit electrical power plants to use biomass such as yard waste, wood, pulp, etc. Total additional costs (assuming nearby supply of biomass) are only 1.4 to 1.8 cents more per kwH.[xxxi] Demand for biomass energy is expected to increase at 8.5% annually.[xxxii] Larger increases are expected in the vehicle fuel market as costs become comparable. Legislative incentives to use biomass fuels and production cost reductions will make biomass fuels more attractive.

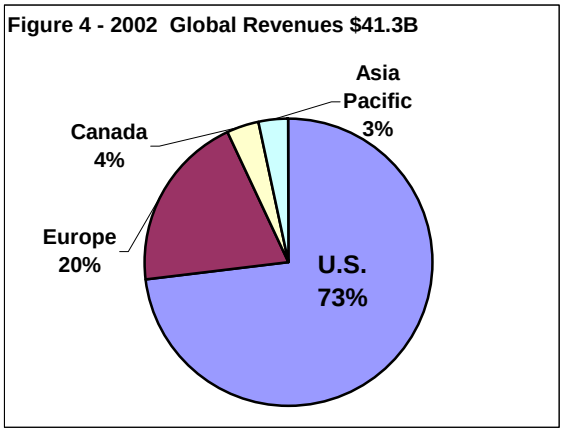
GLOBAL BIOTECHNOLOGY -- COMPETITION AND OUTLOOK

The U.S. remains the world biotech leader, earning nearly three-fourths of all biotech revenues worldwide in 2002.[xxxiii] US dominance thus far in biotech is due in large part to a successful combination of academic research and technology transfer mechanisms, a diverse industrial base in terms of size and scope, a well-established financing network, and stable government R&D funding (see Figures 3 and 4).

While the US currently dominates the global biotech market, other international competitors are making significant investments to try and become players in the global biotech market. Europe is the next largest competitor with 20% of the global market, followed by Canada and the Asia/Pacific region.[xxxiv] While still smaller in total size, the growth rates of Europe and Canada, in terms of revenues and numbers of countries are outpacing the U.S., indicating some level of success in new start-ups in these countries. Likewise, Asia is aggressively pursuing biotechnology in an attempt to translate its success in the IT sector

Figure 3 ***2002***	**Global**	**U.S.**	**Europe**	**Canada**	**Asia Pacific**
Public Co. Data					
Revenues ($,M)	41,369	30,266	8,262	1,466	1,375
R&D Expense ($,M)	22,012	16,272	4,989	555	197
Net Income ($,M)	-12,483	-9,378	-2763	-263	-79
# of Employees	193,753	142,900	33,304	7,785	9,764
Number of companies					
Public	613	318	102	85	108
Private	3,749	1,148	1,776	332	493
Total	4,362	1,466	1,878	417	601

into the biotechnology sector using similar business and government investment models. Asia's large untapped markets, combined with large government investments, lead many analysts to predict that Asia will experience the largest increase in overall growth in the next 10 years.



Increased international competition will create both opportunities and obstacles for the US biotech industry. Access to global markets, especially in Asia, provides tremendous potential for revenue growth. Partnerships will be the likely means by which US firms will pursue these markets. Foreign competitors, in most cases, are not trying to compete directly with existing US products. Rather foreign firms are gaining sales through partnerships with US firms, commercialization of existing technologies that US firms have not pursued, or through focusing on niche markets which have limited attraction to US firms (e.g. traditional Chinese medicines). Foreign governments have in some cases developed policies to restrict or delay US product penetration into their respective domestic markets to give their local companies time to develop products of their own (e.g. EU's bio-agriculture policies). Differing intellectual property protection and enforcement policies also have an impact on US firms' cost/benefit calculations when deciding whether to pursue foreign markets (especially in the case of China). A lack of capital, questionable product safety procedures, and lack of basic science R&D investments will continue to hamper foreign competitors and should enable the US to continue its overall dominance in the global biotech industry for the foreseeable future.

THE U.S. BIOTECHNOLOGY SCIENCE AND ENGINEERING WORKFORCE

From 1991-2001, the number of jobs in the biotechnology industry doubled to 191,000, while jobs in related industries during the same period rose from 230,000 to 535,000. In other words, for every 1 biotech job created, 2 more jobs were created in related support industries.[xxxv] Between 2000 and 2010, science and engineering (S&E) -related occupations are expected to grow by 47%, compared to an overall growth rate of 15 percent for all occupations.[xxxvi] The US biotechnology industry pulls workers from across the entire spectrum of science and engineering (S&E) disciplines: Scientists (55.3%), Science and clinical lab technicians (30.3%), Engineers (8.3%), R&D-focused computer specialists (6.2%) 2002.[xxxvii] (Commerce Department, 2003, 81)

There is no clear consensus in the biotech industry and scientific organizations regarding the availability of qualified U.S. workforce. In Seminar briefings, a number of biotech organizations indicated no particular concern although these organizations tended to be located in close proximity to either academic or government organizations that provided good sources of qualified job candidates. However, several organizations, such as the National Academy of Sciences, the National Science Board, and the Building

Engineering & Science Talent (BEST) partnership, continue to be concerned about shortages, as well as imbalances in the available workforce. There does seem to be common agreement in the literature on three trends: significant numbers of foreign-born workers in the S&E workforce, increased global competition for S&E workers, and fewer native-born Americans entering S&E education or the S&E workforce.

Foreign-Born Workers - A significant portion of the S&E workforce (6-10%) is foreign-born, educated in the US, concentrated in the most highly educated range (college graduate, MAs and PhDs – 17%, 29% and 38% respectively) of positions[xxxviii], and in the US on H1-B visas. Those foreign-born workers are valuable intellectual capital and most remain in the US if they can.[xxxix]

U.S. S&E Workers - The US-born workforce is concentrated in the less educated range of positions[xl] and most growth in US S&E university students has come from women and minorities.[xli] Many U.S. born students either avoid careers in S&E due to the length of study required and the low entry wages[xlii] or because they lack the interest and/or the basic required skills in science and mathematics due to inadequate middle/high school preparation, especially when compared students from other regions, like Asia.

Increased Global Competition for S&E Workers - After 9/11, the US government severely restricted the number of H1-B visas for highly specialized knowledge/highly educated workers.[xliii] At the same time, Asian countries that supply the majority of foreign S&E workforce are building up their own biotech industries and offering incentives to entice their citizens back home.[xliv] . In addition, countries such as Britain, Canada and Australia are competing with the US to attract foreign students and trained S&E talent.[xlv]

Policy implications - The U.S. will need to balance policies aimed at improving the native-born US populations' ability to fill S&E related jobs with the need to maintain a pipeline of foreign-born students and workers, such as greater investment in science through research and development (R&D) and R&D investment incentives for the private sector. In addition, the USG needs to better balance security concerns with the need to maintain or increase the number of H1-B visas and student visas granted to foreign workers and students by streamlining the security clearance process.[xlvi]

SCIENCE AND MATHEMATICS EDUCATION IN THE U.S.

The U.S. is facing a serious challenge in ensuring potential workers have the scientific and technical qualifications and skills necessary to meet industry requirements. The U.S. distantly trails its major competitors like Singapore, South Korea, Taiwan, Hong Kong and Japan on the standardized science and mathematics test, the "Trend in International Mathematics and Science Study (TIMSS)."[xlvii] The poor US performance appears to be due in large part to the way science and mathematics is taught in US schools, partly due to less advanced curricula and partly due to unqualified teachers who are unable to teach these topics in any depth.[xlviii]

Policy implications - More money is not necessarily the solution to the US' education inadequacies but rather finding more effective ways to use the funding now available to develop a highly skilled workforce, including those students who do not attend college. Greater focus on developing more technically qualified teachers education earlier in a student's education is needed. More industry involvement across all levels of education, in developing curricula and programs that stimulate more interest in science and mathematics would ensure that students continue on to college level studies.

INTELLECTUAL PROPERTY

Intellectual property is often the primary asset of biotech companies, especially biotech start-up companies.[xlix] As a result, biotech companies must "create, protect and extract value from their intellectual assets."[l] Patents grant their owner the right to exclude others from making, using, or selling the patented invention in the United States for a period of twenty years from the application filing date.[li] Obtaining a patent is often a lengthy and expensive process, sometimes requiring as much as three years and costing $15,000.[lii] In addition to the protection of particular intellectual assets, biotech firms often use patents as part of their strategic business strategy to deter competitors, attract capital and generate value through licensing of patents. The domestic patent system works relatively well, balancing innovation against competition but there are still areas requiring modification and questionable patents are a significant competitive concern and a threat to innovation.[liii]

Unfortunately, there is currently no single uniform forum to obtain universal patent protection.[liv] Absent the specific application of international agreement, patent protection only extends to the borders of the territory of the country where granted.[lv] As a result, biotech companies must be concerned with obtaining and defending their proprietary rights under the rules of various foreign jurisdictions where they hope to do business.[lvi] Although most developed countries protect intellectual property rights, many of the developing countries fail to provide such protection because they have less incentive to do so.[lvii] This uncertainty injects substantial risk into the industry.

Policy recommendations – Although the current patent system has slowly adapted to the biotech industry, there are further improvements identified in a recent Federal Trade Commission study that would better support the biotech industry in the future:[lviii] (1) provide more resources to the USPTO to obtain more qualified examiners;[lix] (2) provide USPTO examiners with procedural tools to assist in gathering more information on patent claims;[lx] (3) enact legislation to create an administrative post-grant review process to reduce grants of questionable patents and facilitate quick challenges to any granted;[lxi] (4) change the evidentiary standard for challenging the validity of patents from "clear and convincing evidence" to "a preponderance of evidence.";[lxii] (5) tighten "certain legal standards used to evaluate whether a patent is "obvious"[lxiii]; (6) "Consider possible harm to competition – along with other possible benefits and costs – before extending the scope of patentable subject matter."[lxiv]; (7) require <u>all</u> patent filings be published 18 months after filling[lxv]; (8) create intervening or prior user rights to protect parties from infringement allegations that rely on certain patent claims first introduced in a continuing or other similar application.[lxvi]; and (9) require, as a predicate for liability for willful infringement,

either actual, written notice of infringement from the patentee, or deliberate copying of the patentee's invention, knowing it to be patented.[lxvii] These actions would reduce anti-competitive actions by individual companies and reduce costs associated with obtaining patent protection.

In addition, the federal government should take the following actions internationally: First, actively work with international organizations such as the World Intellectual Property Organization (WIPO) to harmonize patent law and establish reciprocity among member nations. As an alternative, the government should negotiate international agreements with countries in major markets, such as the European Union and China, to harmonize laws and allow reciprocity. Second, the government should press countries that are major markets in the biotechnology industry, to vigorously enforce intellectual property rights within their borders.

These recommendations will reduce risk and promote more overall predictability in the industry. They will speed up the patent process, make it more transparent, reduce the number of questionable patents, and reduce the cost of obtaining a patent. This will promote more competition and innovation in the biotechnology industry.

REGULATION AND LABELING OF BIOTECH PRODUCTS

The U.S. biotech industry is the world leader both in pharmaceutical and agricultural biotech and is an important driver for the U.S. economy overall. The use of Genetically Modified Organisms (GMO) in the agricultural sector, that is, seeds, crops and food products for animal and human consumption, is governed by domestic and international regulations, both social (health and safety) and economic (restrictions on trade barriers). In recent years, the use of GMOs has generated debate as certain nations and/or groups have challenged the risk/benefit equation. At the heart of the debate is the controversy over the human and animal safety of GMO crops and food products, and this is being expressed in calls for greater regulation and labeling requirements in some nations.

Although the current focus is on plants and plant products, because those are currently commercially available, the debate will only broaden and intensify when GMO animals, whether for pharmaceutical use or consumption, become commercially viable. While the benefits of GMO plants are largely documented, opponents counter that concerns about "unacceptable unknowns" remain. Those concerns include food safety and the impact on the environment of "unnatural" genes. To date, there has been no scientific evidence to support the contention that GM products are harmful to humans. There has been some evidence of very limited cross-pollination of biotech crops and "natural" crops which the USDA is investigating.[lxviii]

The U.S. regulatory approach to biotech crops and food relies on the notion of "substantial equivalence" and assumes that the engineering process of biotech crops and foods does not warrant special regulation, as it is not an inherently risky process.[lxix] In contrast, the EU regulatory process does not recognize the concept of substantial equivalence of individual products' objective characteristics in regards to GMOs. Rather, the EU has pre-market reviews with case-by-case assessment of risks to human and animal

health, and environmental impact before any GMO or products containing GMOs can be approved. [lxx] The EU has adopted the "precautionary principle" into its consideration of food safety issues and argues that, while decisions should be scientifically based, there are wider societal issues that come into play in policy making on this subject.[lxxi] The notion of a precautionary approach comes from environmental risk analysis and helps authorities deal with "extraordinary" environmental threats. Experts stress however the difference between a precautionary approach to risk analysis and the "precautionary principle" and argue that the current EU approach does not recognize the distinction.[lxxii] The EU has referred to both the WTO Sanitary and Phytosanitary (SPS) Agreement and the Rio Declaration on Development and the Environment (Rio Declaration) in arguing a basis for the introduction of the "precautionary principle" into food safety issues. The SPS Agreement specifies that if scientific evidence is insufficient to establish safety, members may use "precaution" and introduce additional measures.[lxxiii] The Rio Declaration states that the lack of "full scientific certainty" is not an acceptable reason to delay measures to prevent environmental degradation. [lxxiv] The EU linked the WTO SPS notion of "precaution" in risk analysis and the precautionary approach in environmental risk analysis, thus expanding the notion of "full scientific certainly and introduced it into food safety policy.[lxxv] However, experts argue that there is a qualitative difference between risk analysis in the two areas. That is, when compared with environmental risks, most food safety risks are well known, minimal in nature and scope, and of short duration. [lxxvi]

The greatest challenge to the free and fair trade of biotech agricultural products is the effort by some nations or regional groups, such as the EU, and other non-governmental groups to include subjective, non-scientific analysis/elements into the risk and hazard analysis of new products, as well as to extend the notion of "precautionary principle" to the international regulation of GMO crops and food products. Complicating the debate is the European Union's de facto moratorium on the approval of new biotech agriculture products. Although the EU in May 2004 agreed to approve one new GMO corn, this acceptance does not mean that the EU has taken all necessary steps to end the de facto moratorium, which has acted as an unfair trade restriction and appears to be in violation of the EU's World Trade Organization (WTO) obligations. The U.S. and nine other countries have filed suit in the WTO.[lxxvii] In addition, the EU will also require labeling and "traceability" of biotech food and crops, that is, a detailed tracking from seed to producer to retailer of all ingredients in a product, from produce to oils and other additives used in the production process. Thus producers would have to find ways to segregate and trace their products in order to trade. But, even if that proves physically or financially feasible, producers will likely find themselves locked out of supermarket shelves, as retailers fear consumer boycotts and retaliation. This requirement is effectively a trade barrier for US industry. EU policies are also influencing the lesser developed world, in particular Africa, where anti-GMO groups and some EU governments have used fear tactics to dissuade African nations from using GMO products, even in the face of obvious benefits to the local populace (food aid, increased production, solutions to pests and rot, etc). [lxxviii]

Policy recommendations - The USG and U.S. industry must use a multi-pronged approach to address this problem. The USG must use the WTO Dispute Settlement process to challenge unfair trade practices aimed at biotech agriculture. The USG should reverse its current policy of non-signatory/observer status in relevant international

agreements and use the international framework organizations to stop erosion of scientific standards in risk analysis and prevent widespread introduction of the "precautionary principle". And, the U.S. biotech industry should seek cooperative arrangements with key market/potential market in less developed nations that address local agricultural needs (banana/papaya rot, golden rice, etc.) as a way to build confidence and support among non-EU nations.

ETHICAL, SOCIAL AND POLITICAL ISSUES

Biomedical technologies have the potential to relieve human suffering and solve a range of societal problems. However, some of these technologies are controversial, raising ethical, moral and social issues. In order for the industry to reach its full potential, government, academic institutions, politicians, and the general public must effectively address these issues. Two of the most controversial technologies impacting the industry and the U.S. are embryonic stem cell research and human cloning.

Stem Cell Technology - Stem cells are undifferentiated primitive cells with the ability to multiply and differentiate into specific kinds of cells. These cells are prized for research because of their potential to become almost any type of tissue, perhaps one day to be used to treat illnesses or injuries.[lxxix] Stem cells are derived from two sources – embryonic and adult tissue. Some researchers believe the best source of stem cells is derived from human embryonic tissue. The major sources of embryonic stem cells are derived from surplus embryos from in-vitro fertility clinics and are obtained with donor permission. In theory, stem cells can provide an unlimited source of material for cell and tissue replacement and transplantation. These cells potentially could be used to treat a variety of diseases, affecting the health of millions of people worldwide and sharply reducing health care costs.[lxxx] In the United States alone, nearly 130 million patients suffer from diseases that might be helped by embryonic stem cell therapies.[lxxxi] Stem cells could provide replacement cells for patients with diseases such as Alzheimer's, Parkinson's, stroke, diabetes, multiple sclerosis, and blood, bone, and marrow disorders. Embryonic stem cells have already been used to treat diseases in mice and rats that are similar to Parkinson's, multiple sclerosis, and stroke.[lxxxii] Preliminary research also suggests that stem cells could be harnessed to package and deliver gene therapies to specific targets in the body, accelerating advances in another potentially revolutionary field of medicine.[lxxxiii] The technique for harvesting embryonic stem cells requires the destruction of day-old embryos, which some people view as ethically and morally wrong based on their definition of "life." Lawyers and medical ethicists are equally divided on the issue.

The general public is relatively supportive of stem cell research but an important political issue lies in whether or not U.S. taxpayer dollars should be spent to advance technology that is opposed by a segment of society. The federal government has responsibility to oversee and set policy regarding healthcare issues that impact the nation. Therefore, it makes significant public resources available to biomedical researchers each year—over $20 billion in fiscal year 2003 alone—in the form of research grants offered largely through the NIH. In 2001, President Bush approved the current policy, which allows use of federal funding for research on "existing stem cell lines", i.e. 78 lines. The

administration sought to appease stem cell opposition groups while still allowing some limited stem cell research. As of March 2004, at least 16 of the 78 existing stem cell lines approved by President Bush have died or failed to reproduce –making them useless. Most of the others are unlikely to ever become available for disease research.[lxxxiv] . As a result, U.S. federal stem cell research is losing ground to international competitors and private institutions/universities are moving forward without government support.

Scientists and politicians are calling on the president to rescind the current policy limiting federally funded research but the administration at present has no plans to change its policy. Stem cell research in England, Israel, Singapore, South Korea, and China is advancing. Singapore is spending $287 million on a stem cell government biotech center. Chinese researchers have reportedly fused human skin cells with rabbit eggs to produce early stage embryos, which yielded stem cells. The Chinese government is also building a stem cell research center.[lxxxv] Many of these countries do not have the same religious and scientific debate over the definition of "life" and as a result, the associated ethical, political and social issues will not slow them down. Today, most U.S. stem cell research is taking place under privately funded programs at universities such as Stanford, Harvard and the University of California (San Francisco). Most biotechnology firms find the research too expensive and risky to pursue without federal support. Stem cell technologies are roughly 5-10 years away from production release; however ethical considerations are affecting corporate bottom lines today.[lxxxvi]

Cloning Technology - Cloning is a form of reproduction in which offspring are created from the deliberate replication of the genetic makeup of another individual. There are two categories of cloning technology, reproductive and. therapeutic. Reproductive cloning (also referred to as cloning-to-produce-children) involves implanting an embryo into the womb and allowing it to develop into a fetus. To date, only animals have reportedly been used in reproductive cloning. Therapeutic cloning (also referred to as cloning-for-biomedical-research) does not require implanting embryos into the womb, but they grow for a short period of time in the laboratory so stem cells can be harvested.

While most countries reject reproductive cloning, therapeutic cloning-for-biomedical-research is the subject of intense debate. Supporters of therapeutic cloning believe the technology must move forward because of its potential to reverse injuries and illnesses such as Parkinson's disease, Alzheimer's disease, juvenile diabetes, and spinal cord injury. Anti-cloning supporters believe the technology is morally wrong because it also involves the deliberate creation and destruction of human embryos. While most scientists strongly support cloning to make embryonic stem cells, they believe reproductive cloning to be ethically and medically unnecessary.

Policymakers are equally divided on the issue of advancing therapeutic cloning. However, as noted in the embryonic stem cell debate, politicians in general oppose federal funding of cloning research as long as a portion of society objects to the technology. The administration currently prohibits the NIH from issuing federal grants for cloning research while political pressure from new celebrity based private research foundations (Michael J. Fox – Parkinson's disease and Christopher Reeves – spinal cord injuries) is mounting.

Meanwhile, the rest of the world is proceeding with therapeutic cloning research while the U.S. appears to be deadlocked, with industry shying away from the technology due to possible legal action and lack of government support.

Government Role - Stem cell and cloning technologies raise important questions on the role of science, society and the government. Should the government exercise moral and ethical guidelines over the biomedical technology industry and its research? Or, should the industry, scientists and researchers police themselves? Despite repeated congressional efforts, the U.S. currently has no federal laws banning cloning technology. In 2002, the President's Council on Bioethics proposed to the President several public policy options but as yet, no new guidelines have been implemented. The merits of therapeutic cloning are noted but again, no progress to proceed with federally funded research is on the horizon. Supporters fear other countries will take the competitive lead from the U.S. and dominate the field. Others fear the U.S. will experience a reverse brain drain by losing top researchers to foreign countries in their pursuit of scientific freedom. In fact, in February 2004, scientists in South Korea announced that they have created human embryos through cloning and then extracted embryonic stem cells and that success has revitalized the debate between cloning opponents and cloning/stem cell research supporters

BIOLOGICAL WARFARE THREAT AND IMPLICATIONS

"These are times of great challenge for this country. Our country must continue to meet the grave dangers of bioterrorism. We've got to continue to work to help relieve suffering around the world. And we've got to continue to seek cures to terrible diseases. In all of this, we're relying on the skill and conscience of scientists in the field of biotechnology." President George W. Bush, June 23, 2003

Biological terrorism poses a serious challenge to the security of the U.S. An adversary could potentially use bioweapons to instill fear in the American population, kill numerous people, raise serious doubt about the integrity of the U.S. food supply, and drastically affect the U.S. economy. Such an attack on the U.S., the sole superpower, would have an acute global impact. Two recent occurrences, anthrax letters in the postal service and a single cow infected with BSE ("mad cow" disease), serve as examples of small-scale effects bioagents have had upon the U.S.

Diverse Nature of the Threat - One of the great difficulties in countering the threat posed by biotechnology is the dual use nature of the technology. The knowledge of how to produce biological agents is the same knowledge required in producing legitimate biotechnological products. The tools and capabilities to manufacture bioweapons are the same needed for legitimate research as well as commercial development. Virtually all the equipment, technology, and material needed for biological agent research, development, and production are available on the open market. Since biological weapons are relatively cheap, easy to disguise within commercial ventures, and potentially as devastating as nuclear weapons, they are attractive to counter nations with superior conventional or nuclear forces. International agreements attempt to mitigate proliferation of such bio agents and the associated technology but only nation states sign such agreements, not all nations of the world are signatories, and these agreements have no impact upon non-state

actors. The growing concern is that non-state actors will acquire and use a biological weapon, the "poor man's nuclear weapon." Such action is extremely difficult to detect and counter.

International Protocols and the Need to Control Agents and Technologies - The Biological and Toxin Weapons Convention Treaty (BWC) was initiated by the U.S. and established in 1972. The international treaty prohibits or limits the development, production, stockpiling, and transfer of biological weapons through political, legal, and moral efforts. The BWC treaty has served as the cornerstone of the U.S. and international policy concerning worldwide biological development.[lxxxvii] The treaty was successful in limiting the spread of biological weapons throughout most of the world, but in the early 1990s it became apparent that the former Soviet Union and Iraq had developed robust bio programs. The U.S. continues to enforce and strengthen the treaty by elaborate systems of declarations and intrusive inspections of biodefense, biotechnology, and pharmaceutical facilities.

During the Fifth Review Conference of the BWC treaty in 2001, the U.S. voiced serious concerns about treaty compliance by a number of nations. The U.S. withdrew from compliance deliberations on the grounds that the Protocol would be ineffective at preventing cheating yet would impose undue burdens on the U.S. biotechnology and pharmaceutical industries and on U.S. government biodefense programs. The U.S. delegation offered several proposed measures including: criminalizing the acquisition and possession of biological weapons; restricting access to dangerous pathogens and toxins; supporting the WHO's global system for disease surveillance and control; establishing an ethical code of conduct for scientists; and strengthening an existing UN mechanism for conducting field investigations of alleged biological weapons use. Unfortunately, little progress has been made to alleviate the U.S. concerns and give adequate "compliance teeth" to the BWC.[lxxxviii]

National Strategy to Protect Against Biological Terrorism - The U.S. government has taken serious and deliberate steps toward improving the nation's ability to deter and defend against biological threats. Building upon the 2002 National Security Strategy[lxxxix], in June 2002, President Bush signed the Public Health Security and Bioterrorism Response Act of 2002. The legislation addressed four components to enhance the capacity for the U.S. to prevent, identify, and respond to a biologic threat. The components are: tighten controls of biological materials in the U.S. and the inspection of foods entering our ports; recognize the need to improve communication networks between the health authorities and care providers; provide state and local health authorities with the necessary resources to access stockpiles of vaccines and medications in the event of a national biological emergency; recognize the need to further expand the research and development of medications and vaccines with the mutual cooperation of the private industry and governmental resources.[xc]

The Department of Homeland Security (DHS) was established on March 1, 2003. The Science and Technological Support of Homeland Security Division is responsible for developing chemical, biological, radiological, and nuclear countermeasures. The countermeasure efforts involve new surveillance technologies, improved medicines and

vaccinations, smuggling prevention and federal, state and local response plans.[xci] Some highlights of efforts in 2003-2004 include increase in CDC-trained clinicians, strengthening of the Strategic National Stockpile (repository for antibiotics, antidotes, antitoxins, etc.) to support state and local public health agencies during national emergencies, establishment of BioWatch environmental monitoring mechanism, and increase in proposed financial and human resources. In 2003, the President's budget reflected a significant increase to fund these critical areas and the 2004 budget further sustains these initiatives. In March 2004, Health and Human Services announced the establishment of the National Science Advisory Board for Biosecurity (NSABB). The NSABB will advise all federal departments and agencies that conduct or support life sciences research categorized as "dual-use" and will be managed by the National Institute of Health.[xcii]

Policy recommendations - The biotechnology industry is making tremendous strides. The U.S. government must emphasize a comprehensive understanding and approach of the recent research, development, future capabilities, and the threats in biotechnology. The U.S. needs an overarching framework for the orchestration of our biological S&T, medical, and warfare programs.

The U.S. needs to continue engagement in multi-lateral forums such as the BWC and the UN to strengthen compliance of the BWC treaty, develop international controls and protocols to protect against BW state and non-state actors, and control "dual-use" technologies and capabilities.

The Homeland Security Council must finalize and publish a Presidential Directive that outlines an operational framework for our bio-defense strategy. This will bring together the components of planning, intelligence, communications, medical and environmental surveillance, laboratory analysis, and medical countermeasures.

DHS should develop measures of merit for each component area and determine target capabilities. How many labs are enough? What and how many cities need a BioWatch capability? What type and how much of agricultural surveillance/analysis is required? Is the strategic national stockpile sufficient? Agencies must work together to prioritize, leverage and share scientific advances.

FUTURE OF THE BIOTECHNOLOGY INDUSTRY

Future demographic changes are perhaps the most important catalyst that will spur strong growth in biotech sales and revenue. Over the next 20 years, US life expectancy is expected to increase from 65.4 years to 69.1 years, the global population will rise from 6.3 billion people to 7.9 billion people, and infant mortality rates will decrease from 55.6 deaths per 1000 births to 37.4 deaths per 1000 births worldwide. According to the U.S. Census Bureau, the number of Americans between the age of 45 and 64 years old will increase 18% between 2003 and 2010 as compared to an overall population growth rate of 6%[18]. The trends of a larger population of elderly people, prolonged life spans, and growing populations will combine into the "perfect market" for sustained growth in the

biotech industry.

At the same time, the combination of greater life science knowledge and the application of information technology to basic research will continue to reduce the cost and time associated with R&D through such synergistic technologies as genetic micro-arrays. The U.S. Department of Defense is already enjoying the benefits of this synergy through the joint efforts of the U.S. Army Medical Research Institute of Infectious Diseases and the U.S. Army High Power Computing Center in which a joint team screened 35 million potential drug molecules against the smallpox vaccine to significantly narrow the candidate list for future lab experimentation[19]. Other indicators point towards future growth in the biotech industry including continued growth in the number of products in the FDA pipeline and the number of biotech patent submissions. According to the leading biotech trade association, there are 371 drug candidates in the late-stages of FDA approval, more than have ever been in the pipeline before[20]. At the same time there were over 33,000 patent applications in 2002 alone[21] and patent submissions are continuing at a steady pace.

Equally as exciting and promising, is the synergistic combination of biotechnology and nanotechnology, or as some call it, nanobiotechnology. Nanotechnology, which became a national priority in 2000 with the birth of the National Nanotechnology Initiative (NNI), is the next stop in the miniaturization path that gave us breakthroughs such as microelectronics and microchips in the computer industry. Nanotechnology stands ready to have an enormous impact on biotechnology and medicine. Nanotechnology is the technological application of *nanoscience*, the study of physical, electromagnetic, and biological principles and systems at the nanometer scale, with the goal of developing unique applications in a range of microscopic realms (NSF). [xciii] In general, nanotechnology is the scientific field that builds devices and structures at the nanoscale, which is roughly one-thousandth the width of a human hair.

The *nanomaterials* and *nanodevices* under development have the design features on a molecular scale that have an enormous potential to interact directly with cells and macromolecules. Conversely, biotechnology, which involves the manufacturing on a molecule-by-molecule basis, has the potential to facilitate the manufacture of materials with *nanoscale* architecture. As nanotechnology and biotechnology converge, they present the ability to produce *nanoscale* devices that employ biological principles. This unique combination of scientific development is an emerging reality that shows promise over the next several decades in molecular machinery, materials and fabrication, biological sensors, computing, and medicine. For example, nanomedicine is the application of nanotechnology Focusing on the monitoring, repair, and construction and control of human biological systems at the molecular level to prevent and treat disease in the human body. (Frietas)[xciv] More advanced uses of nanotechnology might involve implanted devices to dispense drugs or hormones as needed in people with chronic imbalance or deficiency states.

CONCLUSION

Biotechnology has the potential to revolutionize all aspects of our daily of life over the next two decades, in much the same way information technology did during the previous two decades. Biotechnology is still an immature industry that has yet to reach its full

potential, but it is already an important driver for the U.S. economy overall. It presents the U.S. with a tremendous opportunity to address many of the country's most pressing defense, health, and economic issues. It also holds promise for improvement in global health and welfare but only to the degree that other nations are willing to utilize the technology and are successful in their respective biotechnology initiatives.

Biotechnology is greatly affected by government investment in basic science, government regulation, and the government product approval processes. These factors drive a unique business model. The synergy between U.S. government policies and funding, academia, and the industrial base provides the U.S. with a unique competitive advantage and is a primary reason the U.S. has been able to quickly become the global leader in biotechnology. While the recent recession temporarily cooled the rapid growth of biotech industry, it did not stifle long-term growth in revenues or sales, nor prevent sustained long-term growth. Demographics and a geometric expansion of biotech applications will fuel the biotech market well into the coming century.

The U.S. is the world leader in the biotechnology industry in all aspects – the number of companies, size of the research base, number of products and patents, and level of revenue. While the U.S. is the dominant player in today's biotechnology market, other countries in general, and Asia in particular, are actively investing in government sponsored programs to increase their market share and reduce the US dominance overall. The U.S.' future lead in biotechnology is threatened by a potential shortage of U.S. scientists and engineers, an increasing global demand for scientists, fewer U.S. college graduates in math and science, and tighter U.S. visa restrictions on foreign students and scientists.

Unfortunately, biotechnology's potential for improving the quality of life in the U.S. and the rest of the world is tempered by the risk of enemy or terrorist use of bioagents and/or bioweapons against the US or its allies. The potential dual use of biotechnology complicates the effort to craft effective non-proliferation policies and mitigate bio-weapons threats. As biotechnology continues to mature as a technology and industrial sector, policy makers at the U.S. and global level must continue to refine global non-proliferation and counter-proliferation regimes to ensure biotechnology's potential for mis-use does not outweigh its ability to address the world's most pressing needs.

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[lvii] James D. Gaisford, Robert Tarvdas, Jill E. Hobbs and William A. Kerr, *Biotechnology Piracy: Rethinking the International Protection of Intellectual Property*, Canadian Journal of Agricultural Economics 50 no 1 15-34 March 2002. at 2. China is an example of the problem faced in the developing world. China instituted an intellectual property legal regime in 1985. see generally, *Patent Protection to Be Strengthened*, Financial Times Information, April 23, 2003. However, like many developing countries, enforcement has been a problem. However, there are signs the Chinese government realizes the need to enforce such rights and has taken some steps to strengthen enforcement. See generally, *China Signs Patent Protection Protocol with Intellectual Property Body*, Financial Times, May 22, 2002. On 22, May 2002 The State Intellectual

Property Office of China signed a protocol with the World Intellectual Property Organization (WIPO) to improve mutual efforts to protect copyrights and patents. Likewise, on 10 October 2003, the Chinese government created a China Patent Protection Association under the State Intellectual Property Rights Bureau to enforce intellectual property rights in the country. Amanda S. Reid, *Case Note and Comment: Enforcement of Intellectual Property Rights in Developing Countries: China as a Case Study*, 13 DePaul-LCA J. Art & Ent. L 63.

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[lx] Ibid at page13. a. Amend PTO regulations to require that, upon the request of the examiner, applicants submit statements of relevance regarding their prior art references; b. Encourage the use of examiner inquiries under Rule 105 to obtain more complete information, and reformulate Rule 105 to permit reasonable follow-up; c. Implement the PTO's recommendation in its 21st Century Strategic Plan that it expand its "second-pair-of-eyes" review to selected areas; and d. Continue to implement the recognition that the PTO "forges a balance between the public's interest in intellectual property and each customer's interest in his/her patent and trademark."

[lxi] Ibid at page 8. Although recent legislation took steps to solve this problem, the most effective way to challenge a questionable patent is still litigation, which is too costly in most cases. Testimony reported that a biotechnology case to challenge a patent can cost as much as five to seven million dollars and take two to three years.

[lxii] Ibid at page 9 and ftn. 25, at page 10. This is based upon the fact that under current precedent once a patent claim is filed it is effectively presumed valid unless the PTO can prove otherwise. "The PTO works under a number of disadvantages that can impede its ability to reduce the issuance of questionable patents. Perhaps most important, the courts have interpreted the patent statute to require the PTO to grant a patent application unless the PTO can establish that the claimed invention does not meet one or more of the patentability criteria. Once an application is filed, the claimed invention is effectively presumed to warrant a patent unless the PTO can prove otherwise." "Also, the PTO's resources are inadequate to effectively screen questionable patents Patent applications have doubled over a twelve year period and rise about a 10% per year. There are approximately 300,000 filings a year or about 1000 per day…Each examiner has about 8-25 hours to read and understand each application, search prior art, evaluate patentability, communicate with the applicant, work out necessary revisions, and reach and write up conclusions."

[lxiii] Ibid at page 10. "The courts have developed a variety of tests to evaluate the obviousness of a claimed invention. Two in particular – the "commercial success test" and "the suggestion test" – require more thoughtful application to weed out obvious patents." Specific recommendations in this regard are: "a. [I]n applying the "commercial success" test, 1) evaluate on a case by-case basis whether commercial success is a valid indicator that the claimed invention is not obvious, and 2) place the burden on the patent holder to prove the claimed invention caused the commercial success. b. In applying the "suggestion" test, assume an ability to combine or modify prior art references that is consistent with the creativity and problem-solving skills that in fact are characteristic of those having ordinary skill in the art."

[lxiv] Ibid at page 14. The report's rationale, in part is: "The constitutional intention that patents "promote the Progress of Science and useful Arts" should be taken into account in interpreting the scope of patentable subject matter under Section 101. Decision makers should ask whether granting patents on certain subject matter in fact will promote such progress or instead will hinder competition that can effectively spur innovation. Such consideration is consistent with the historical interpretation of patentable subject matter, which implicitly recognizes that granting patent protection to certain things, such as phenomena of nature and abstract intellectual concepts, would not advance the progress of science and the useful arts. For future issues, it will be highly desirable to consider possible harms to competition that spurs innovation – as well as other possible benefits and costs – before extending the scope of patentable subject matter."

[lxv] Ibid at page 15. "A relatively recent statute requires all patents – except those only filed domestically- be published 18 months after filing….This recommendation would extend the requirement to all patent filings. This increases business certainty and reduces the problem of so called "submarine patents".

[lxvi] Ibid at page 16. This would help prevent an anti-competitive practice of "opportunistic broadening of claims" to capture competitor's products. "After publication of its patent application, an applicant may continue to amend its claims. Through this claim amendment process, a patent that states broader claims

than those published at 18 months can still emerge. If the applicant uses procedures such as continuing applications to extend the period of patent prosecution, the potential for anticompetitive hold up increases. Indeed, several panelists asserted that some applicants keep continuing applications pending for extended periods, monitor developments in the relevant market, and then modify their claims to ensnare competitors' products after those competitors have sunk significant costs in their products."

[lxvii] Ibid at page 6. "It is troubling that some businesses refrain from reading their competitors' patents because they fear the imposition of treble damages for willful infringement. Nonetheless, infringers must not be allowed to profit from knowingly and deliberately using another's patented invention due to a low likelihood that the patent holder can afford to bring suit or obtain substantial damages. The FTC's recommendation would permit firms to read patents for their disclosure value and to survey the patent landscape to assess potential infringement issues, yet retain a viable willfulness doctrine that protects both wronged patentees and competition."

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